# A Bidirectional Relationship between Depression, Anxiety and Migraine Headache

*Thesis*

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in Neuropsychiatry

*By*

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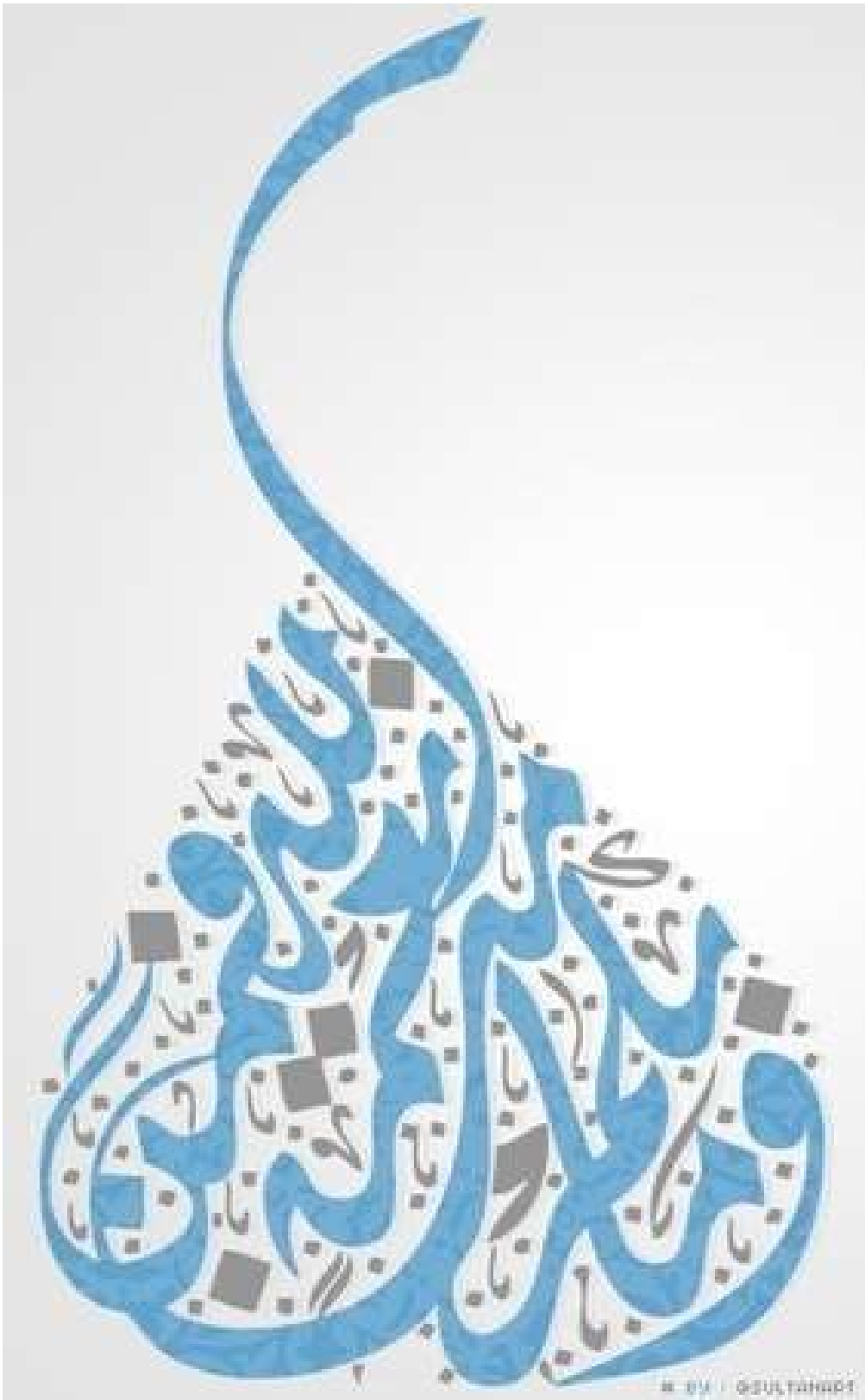
# *Dedication*

*Dedicated to the one who raised me, to the blessing of my life,*

*To My Mother.*

*Dedicated to the soul of my beloved father, who supported me to reach.*

*Dedicated to the soul of my dear friend Habiba, who taught me the meaning of life and eternity.*



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| | |
|---|---|
| ***WHO*** | *World Health Organization* |
| ***NIMH*** | *National Institute of Mental Health* |
| ***ICHD*** | *International Classification of Headache Disorders* |
| ***GAD*** | *generalized anxiety disorder* |
| ***OCD*** | *obsessive-compulsive disorder* |
| ***PD*** | *Panic disorder* |
| ***MDD*** | *Major depressive Disorder* |
| ***BD*** | *Bipolar Disorder* |
| ***OR*** | *odds ratio* |
| ***5-HT*** | *5-hydroxytryptamine* |
| ***CSD*** | *cortical spreading depression* |
| ***NO*** | *nitric oxide* |
| ***CGRP*** | *Calcitonin gene-related peptide* |
| ***NGF*** | *nerve growth factor* |
| ***BDNF*** | *brain-derived neurotrophic factor* |
| ***NT*** | *neurotrophin* |
| ***TrkB*** | *Tropomyosin receptor kinase B* |
| ***NTR*** | *neurotrophin receptor* |
| ***GDNF*** | *glial cell line-derived neurotrophic factor* |
| ***mRNA*** | *Messenger RNA* |
| ***miRNA*** | *Micro RNA* |
| ***HPA axis*** | *hypothalamic-pituitary-adrenal axis* |
| ***SGK1*** | *serum- and glucocorticoid-inducible kinase 1* |
| ***MZ*** | *Monozygotic* |
| ***IHS*** | *International Headache Society* |
| ***MS-Q*** | *Matriculating Student Questionnaire* |
| ***QoL*** | *quality of life* |
| ***MIDAS*** | *Migraine Disability Assessment Questionnaire* |
| ***HIT*** | *Headache Impact Test* |

| | |
|---|---|
| ***DSM*** | *diagnostic and Statistical Manual of Mental Disorders* |
| ***BDI*** | *Beck depression inventory* |
| ***PHQ*** | *Patient Health Questionnaire* |
| ***PTSD*** | *Post Traumatic Stress Disorders* |
| ***PCL*** | *Post Traumatic Stress Disorders Checklist* |
| ***SD*** | *Standard Deviation* |
| ***MWD*** | *Migraines with depression* |
| ***MC*** | *migraine without depression as controls* |
| ***DSM-IVPC*** | *Diagnostic and Statistical Manual of Mental Disorders, Primary Care Version* |
| ***MDE*** | *Major Depressive Episode* |
| ***HRQoL*** | *Health-related Quality of Life* |
| ***FRAMIG*** | *population-based postal survey carried out in France* |
| ***SF*** | *Short form* |
| ***HADS*** | *Hospital Anxiety and Depression Scale* |
| ***M*** | *Male* |
| ***F*** | *Female* |
| ***PPS*** | *painful physical symptoms* |
| ***US*** | *United states* |
| ***BP*** | *Bodily pain* |
| ***PF*** | *Physical function* |
| ***TCAs*** | *Tricyclic antidepressants* |
| ***AEs*** | *Adverse effects* |
| ***SSRI*** | *Selective serotonin re-uptake inhibitors* |
| ***SNRI*** | *Serotonin–norepinephrine reuptake inhibitors* |
| ***FDA*** | *Food and Drug Administration* |
| ***wk*** | *Week* |
| ***CBT*** | *cognitive-behavioral therapy* |
| ***PHQ*** | *Patient Health Questionnaire* |
| ***GABA*** | *gamma-aminobutyric acid* |
| ***U*** | *unit* |
| ***VNS*** | *vagus nerve stimulation* |
| ***rTMS*** | *repetitive transcranial magnetic stimulation* |
| ***MST*** | *magnetic seizure therapy* |

| | |
|---|---|
| ***DBS*** | *deep brain stimulation* |
| ***SCID*** | *Structured Clinical Interview* |
| ***HAM-A*** | *Hamilton Rating Scale for Anxiety* |
| ***n*** | *Number* |
| ***P*** | *p-value* |
| ***r*** | *r-value* |
| ***SADS-L*** | *Schedule for Affective Disorders and Schizophrenia-Lifetime* |

# Introduction

# Introduction

**Depression** is a significant contributor to the global burden of disease and affects people in all communities across the world. Today, depression is estimated to affect 350 million people. The World Mental Health Survey conducted in 17 countries found that on average about 1 in 20 people reported having an episode of depression in the previous year. Depressive disorders often start at a young age; they reduce people's functioning and often are recurring. For these reasons, depression is the leading cause of disability worldwide in terms of total years lost due to disability. Almost 1 million lives are lost yearly due to suicide, which translates to 3000 suicide deaths every day. For every person who completes a suicide, 20 or more may attempt to end his or her life **(WHO, 2012***)*.

Depression is a disorder of the brain. There are a variety of causes, including genetic, environmental, psychological, and biochemical factors. Depression usually starts between the ages of 15 and 30, and is much more common in women **(NIMH, 2013).**

**Migraine** is a common disabling primary headache disorder. Epidemiological studies have documented its high prevalence and high socio-economic and personal impact. In the Global Burden of Disease Survey 2010, it was ranked as the third most prevalent disorder and seven-highest specific cause of disability worldwide. Migraine has two major subtypes: migraine without aura is a clinical syndrome characterized by headache with specific features and associated symptoms.

Migraine with aura is primary characterized by transient focal neurological symptoms that usually precede or sometimes accompany the headache. Some patient also experience a premonitory phase, occurring hours or days before the headache, and headache resolution phase. Premonitory and resolution symptoms include hyperactivity, hypoactivity, depression, craving for particular foods, repetitive yawning, fatigue and neck stiffness or pain (**ICHD, 2013).**

Numerous epidemiological and clinical research studies have confirmed elevated risk of mood and anxiety disorders in migraine as well as in chronic daily headache. The studies examining the relationship between migraine and major depression have odds ratios varying from 2.2 to 4.0 **(Lipchik and Penzien, 2004)**. Moreover, persons with migraine with or without major depression are at higher risk for suicide attempts than those without any history of migraine. One study found migraineurs 4 to 5 times more likely to suffer from generalized anxiety disorder (GAD) and 5 times more likely to suffer from obsessive-compulsive disorder (OCD). There appears to be a bidirectional relationship between migraine and depressive disorder and between migraine and panic disorder (PD). Migraine increases the risk for first onset of both major depression and PD, and depression and panic increase the risk for the first onset of migraine. **(Bresalu, 1998) (Baskin et al., 2006).**

Psychiatric comorbidity, especially depression and anxiety, has been well documented in patients with primary headache disorders. The presence of psychiatric comorbidity in headache patients is associated with decreased quality of life,